REMARKS

I. Status of the Claims

Claims 1 and 22-35 are currently pending. Upon entry of this amendment, claims 25 and 31-33 are amended and claims 1, 22-24 and 27-30 canceled without prejudice or disclaimer. Applicants reserve the right to reintroduce the unamended or canceled claims in this or another application. New claims 36-38 are introduced upon entry of this amendment. Claims 25-26 and 31-38 are thus pending following entry of this amendment.

Claim 25 has simply been converted to independent form. The new claims are supported throughout the specification including, for example, the following sections:

Claim 36: page 19, lines 1-10 and the examples;

Claims 37 and 38: page 37, lines 7-8

II. Objections to the Specification

The embedded hyperlinks on pages 12 and 79 have been deleted.

The specification is objected to for allegedly attempting to incorporate essential material present in non-U.S. patent documents. No indication, however, is provided as to why the documents are deemed to be essential to the practice of the currently claimed invention. Clarification is requested.

The trademark on page 77 has been capitalized as requested.

III. Claim Rejections under 35 U.S.C. §112, First Paragraph

A. New Matter

The Office Action asserts that the application is only enabled for screening methods that utilize B cells. Without agreeing with this conclusion, the claims have been amended to indicate that the presently claimed methods are conducted with B cells to advance prosecution of important subject matter.

It is also asserted in the Office Action that the specification lacks support for the concept of screening drug candidates to determine whether they are "potential

immunosuppressants." The current claims have been amended to delete this phrase and instead refer to methods that can be utilized to screen drug candidates to identify those that are potential modulators of B cell tolerance. This rejection is thus rendered moot. It is, nonetheless, noted that the specification provides support for methods of identifying modulators of B cell tolerance (see, e.g., page 36, line 27 to page 37, line 2; and page 37, line 21-23).

B. Written Description

Claims 1 and 22-35 are rejected because it is argued that the specification does not provide specific examples of drug candidates identified by the claimed screening methods. The Office Action states that an invention such as a chemical genus requires a precise definition (e.g., chemical structure, formula or name). Because such details are alleged to be absent from the specification, it is concluded that the claimed subject matter has not been described to convey that the inventors had possession of the claimed invention at the time the application was filed.

In response it is noted that the fundamental inquiry in evaluating whether the written description requirement has been satisfied is whether the specification conveys with reasonable clarity to those skilled in the art, as of the filing date sought, that applicant was in possession of the *invention as now claimed* (see, e.g., MPEP 2163.02). Because the present claims are directed to *screening methods* to identify active drug candidates rather than the drug candidates themselves, the details the Office requires are not necessary to practice the currently *claimed invention*. More specifically, the identity of specific modulators that can be detected by the current screening methods are not required to practice the method. While the identity of such modulators may be necessary to satisfy the written description requirement for claims directed to modulators per se, one can conduct the current screening methods without knowing in advance the identity of active modulators. In fact, the very goal of a screening method is to identify as yet unknown active modulators. So requiring applicants to identify active compounds before a screening method is conducted is unfair because it requires applicants to provide the very information that the claimed method is designed to provide.

IV. Claim Rejections under 35 U.S.C. §112, Second Paragraph

Claims 1 and 22-35 are rejected under 35 U.S.C. §112, second paragraph because the phrase "potential modulator of B cell activation" or "potential modulator of B cell tolerance" is said to be indefinite.

In response, it is submitted that in the context of drug screening that the word "potential" has a recognized meaning in the art. Those of ordinary skill recognize that referring to a compound as having "potential" activity means that the compound has demonstrated some activity in a screen or screens, but that this activity has not been confirmed by further screening. In such circumstances, it is conventional in the art to refer to such compounds as potentially have a desired activity (e.g., as potential modulators). In fact, the concluding comments in paragraph 15 of the Office Action dealing with this particular rejection reflects this well-known understanding. So one of ordinary skill reading the current claims would understand that the drug candidates identified by the claimed screening methods are considered potential modulators of B cell tolerance because of their ability to affect the expression level of one more of the recited genes, but that additional testing may be required to confirm such activity.

V. Claim Rejections under 35 U.S.C. §102

Claims 1, 22-23 and 31-33 are rejected under 35 U.S.C. 102(b) as being anticipated by Foulkes et al. (U.S. Patent No. 5,580,722).

In response, it is noted that the claims have been amended to focus on the method described in claims 25 and 26, which the Office deems to be patentable over Foulkes. This amendment is made solely to advance prosecution of important subject matter and should not be construed to indicate agreement with the grounds for rejection as presented in the Office Action with respect to the canceled claims. As noted above, this amendment is made without applicants disclaiming the right to pursue the original claims in another application.

VI. Claim Rejections under 35 U.S.C. §103

Claims 1 and 22-35 are rejected under 35 U.S.C. §103 as obvious over PCT publication WO 97/10365 (Lockhart) in view of Groseveld et al. (U.S. Patent No. 6, 110,666;

"Groseveld"). The Office Action takes the position that Lockart discusses general methods for conducting expression analysis but lacks a discussion of the specific genes recited in the current claims. Grosveld, however, is said to discuss CD72 as a marker expressed on the surface of pre-B cells. It is thus concluded that it would be obvious for one of ordinary skill in the art to use the screening methods discussed in Lockart to identify modulators of CD72 which is referred to in Groseveld because Lockart teaches that genes of interest in screening methods include those that are involved in immune responses.

Applicants disagree with this analysis because it does not account for each and every element of the claimed invention as required to establish a prima facie case of obviousness. First of all, the claims as currently pending do not simply require that the drug candidate be a modulator of a B cell state, but that a drug candidate that is found to affect expression of one or more of the recited genes be *identified* as a modulator of B cell tolerance. There is no discussion in the cited references that would enable one of ordinary skill to identify modulators in this way as neither of the cited references include any discussion whatsoever of the genes that are important in B cell tolerance, or any of the other states that B cells can exist in for that matter.

The specification identifies genes that are expressed in a variety of different B cell states, including, for example, naïve, activated, immunosuppressed, tolerant and resting states (see, e.g., page 16, lines 8-11). Even if one assumes, for the sake of argument, that those of skill in the art could conduct a screening method to identify modulators of B cells based on the discussion in the two cited references, they would NOT be able to identify whether such compounds were potential modulators of B cell tolerance, as compared to any of the many other B cell states (e.g., naïve, activated, immunosuppressed and resting states). It is only with the information such as provided in the current application that such distinctions can be made. So lacking this information, one of skill could not conduct one of the steps in the current methods. For this reason alone it is submitted that the obviousness rejection should be withdrawn.

Claims 26 and 36 are further distinguished from the combined teachings of the cited references. Claim 26, for example, requires:

(a) determining (i) whether expression of carb anh II, CD72, SATB1, ApoE, CD83, cyclin D2, Cctq, MEF-2C, TGIF, Aeg-2, lck, E2-20K, pcp-4, kappa V, neurogranin,

NAB2 and/or gfi-1 is *increased* in the test cell relative to the control cell, or (ii) whether expression of Ly6E.1, vimentin, hIP-30, TRAP, bmk, CD36, Evi-2 and/or c-fes is *decreased* in the test cell relative to the control cell; and

(b) identifying the drug candidate as a potential modulator of B cell tolerance if the expression level of a gene listed in (i) is increased and/or the expression level of a gene listed in (ii) is decreased.

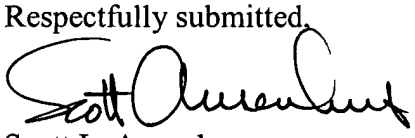
The cited references, even when combined, do not teach or suggest a method that involves determining whether the specified genes in (a) are increased or decreased. Nor do they teach or suggest identifying the drug candidate as a potential modulator of B cell tolerance based upon the criteria listed in (b).

Claim 36 describes methods that are similar to those described in claim 26 but involve identifying a drug candidate as a potential modulator of B cell tolerance only if the expression level of a gene listed in (i) is increased AND the expression level of a gene listed in (ii) is decreased. Identification of the drug candidate based upon these criteria are not taught or suggested in the cited art.

So for all these reasons, it is submitted that the cited references, even when combined, fail to teach or suggest several aspects of the currently claimed invention. As such, a prima facie case of obviousness has not been established. Accordingly, it is requested that this rejection be withdrawn.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 303-571-4000.

Respectfully submitted,



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